

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket: MAOR=2

In re Application of:)	Conf. No.: 8228
)	
Zeev MAOR)	Art Unit: 1617
)	
Appln. No.: 09/582,522)	Examiner: G. C. Yu
)	
Filed: August 24, 2000)	Washington, D.C.
)	
For: A GEL COMPOSITION FOR)	
SKIN CARE AND PROTECTION)	
AND A METHOD FOR...)	

DECLARATION #4 UNDER 37 CFR § 1.132 OF SHLOMO MAGDASSI

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Randolph Building, Mail Stop Amendments
401 Dulany Street
Alexandria, VA 22314

Sir:

I, Shlomo Magdassi of 36 Hanered Street, Jerusalem,
Israel, an Israeli citizen, declare and state as follows:

I am a Professor at the Hebrew University in
Jerusalem.

My *Curriculum Vitae* was previously submitted in
connection with my first declaration filed November 26, 2003.

I am one of the inventors of the above identified
application.

I have been informed that the examiner has
interpreted my declaration #2 filed July 6, 2004, as opining

that the problem of precipitation was due to the addition of hydrophobic agent to Dead Sea water. It is further my understanding that the examiner has taken the position that it is well known that nonionic solublizers have been used for the purpose of making clear gels that contain lipophilic active agents.

A number of experiments have been conducted by me or under my direct supervision so as to provide physical evidence proving that these statements of the examiner are not accurate and that the results of the present invention would not have been predictable from any reading of the prior art cited by the examiner. These will be discussed in detail below.

Submitted herewith is a spreadsheet showing the parameters and results for all of the experiments that were set forth in my declarations #1 and #2, as well in the present declaration #4. Each of the experiments in the tables of declarations #1 and #2 is given an example number and its own line in the attached spreadsheet. The example numbers are listed consecutively for all of the declarations for ease of reference. Thus, in the attached spreadsheet, Examples 1-70 were in declaration #1 (filed November 26, 2003), Examples 71-160 were in declaration #2 (filed July 6, 2004), and Examples 161-201 are new to the present declaration. Photographs of vials containing the resulting solutions or gels are also

submitted herewith and are cross-referenced to the spreadsheet.

The new experiments of this declaration #4 have been conducted by me or under my direct supervision, varying the parameters of the present invention and, in some cases, attempting to replicate the data in the prior art. In some of these experiments, no gelling agent is used so solutions are obtained rather than gels. However, if a solution is turbid, it is less likely that a corresponding gel would be clear.

First of all, as to the examiner's statement that my previous declarations stated that the problem of precipitation was due to the addition of hydrophobic agent to Dead Sea water, this was not the message that I had intended to convey in my previous declarations. It can be seen from declaration #1, for example, that experiments 1-40 were conducted without any hydrophobic agent at all, and yet when Dead Sea water is used with an anionic surfactant, a precipitate was always obtained (note, experiments 2-5, 7-10, 12-15 and 17-20). On the other hand, when the same amounts of Dead Sea water are present, but using a nonionic surfactant transparent solutions are yielded (see experiments 22-40). Similar results can be seen by comparing experiments 162-164 with experiments 176-178. It is true that the addition of hydrophobic agent exacerbates the problem of obtaining a clear solution or gel,

but no fair reading of my first and second declarations, particularly when taking into consideration the experiments added in the present fourth declaration and my statements herein, would lead to the conclusion that the problem being solved by the present invention was how to add hydrophobic agent to Dead Sea water and maintain a clear gel. The problem is also how to get a clear gel using the extremely high salt concentrations of Dead Sea water even without hydrophobic agent and also how to do so when the problem is exacerbated by the further addition of hydrophobic agent.

As to the examiner's statement that it is well known that nonionic solublizers have been used for the purpose of making clear gels that contain lipophilic active agents, the examiner's attention is invited to the comparisons of experiments 172 and 200 with 201. It can be seen that when using normal sea water, the gel is clear whether a cationic surfactant is used or a nonionic surfactant. The fact that Flick discloses that a formulation with a hydrophobic agent and a nonionic solublizer is clear does not teach those of ordinary skill in the art that the same formulation with an ionic solublizer would not have been clear. That is not a conclusion that can be drawn from Flick, in my opinion, and the comparative experiments 200 and 201 support this conclusion.

That the problem is unique to Dead Sea water and its extremely high salt concentration is evident not only from the results of declaration #1, discussed above, but also from the experiments presented for the first time with this declaration #4. First, attempts were made to repeat Example 1 of the Malençon reference. However, we found that it was impossible to obtain a clear, i.e., substantially transparent, gel as sodium alginate will always cause precipitation of sea water as well as Dead Sea water (see experiments 193 and 198). Thus, it is impossible to obtain a clear gel using the technique of Malençon. It should be noted that this is not necessarily contradictory to the results of Malençon, as Malençon states that the product is "practically colorless." The word "colorless" does not necessarily mean that it is transparent or clear. It means only that it has no color. It could still be turbid.

In order to allow better comparisons, 0.4% Natrasol (hydroxyethyl cellulose) was substituted as the gelling agent and comparisons were made substituting various concentrations of Dead Sea water for the filtered sea water of Malençon. First of all, it can be seen from experiments 161-164 that there is no problem in getting a clear solution of sea water with 6% benzalkonium chloride (BC) as the surfactant (experiment 161). BC is a cationic surfactant. On the other

hand, one obtained only a semi-transparent solution at 30% Dead Sea water (experiment 162) and turbid solutions using 50% and 80% Dead Sea water (experiments 163 and 164). Even when a hydrophobic agent is added to the sea water and BC surfactant, the solution remains clear (experiments 165 and 166) while the same experiment with 75% Dead Sea water yields a turbid solution. One also obtains a turbid solution using 50% Dead Sea water (experiment 171).

Similarly, when using Natrasol as a gelling agent, the gel is clear using a cationic surfactant with normal sea water (experiment 172), while the gel is turbid when 50% or 75% Dead Sea water is used (experiments 173 and 174).

On the other hand, when a nonionic surfactant is substituted, in the absence of gelling agent or hydrophobic agent, the solutions are clear even when up to 80% Dead Sea water is used (see experiments 175-178). The solutions remain clear even when hydrophobic agent is added (see experiments 179-181). When Natrasol is added as a gelling agent, the gel is also clear using 50% and 80% Dead Sea water (see experiments 182-183).

For direct comparison of Dead Sea water using nonionic surfactant as compared to cationic surfactant, compare experiments 184 and 185, experiments 186 and 187,

experiments 188 and 189, and then experiments 190 and 191. Also compare experiments 194 and 195, and 196 and 197.

Note that Natrasol is Natrasol HHBR (hydroxy ethyl cellulose). In the surfactant column the letter in parenthesis following the amount and identity of the surfactant is the kind of surfactant that it is, A being anionic, C being cationic and N being nonionic. As stated in my declaration #1, many of the results were analyzed in a turbidimeter, with the turbidity quantified in units of NTU (Standard turbidity units), wherein a substantially clear composition was considered a composition having a NTU below 100.

Accordingly, from the 201 experiments reported in my declarations #1, #2 and #4, and the additional experiments reported in my declaration #3, it can be seen that the references of record would not make it obvious to one of ordinary skill in the art that the problem of avoiding turbidity when forming a gel with Dead Sea water, with or without the presence of hydrophobic agent, could be solved by the use of nonionic surfactant.

I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge

In re of Appln. No. 09/582,522

that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

6-July-08

Date

/Shlomo Magdassi/

Shlomo Magdassi

EX. NO. PHOTO X-REF WATER SURFACTANT GELLING AGENT HYDROPHOBIC AGENT GEL/SOLUTION CLARITY NTU

DECLARATION #1

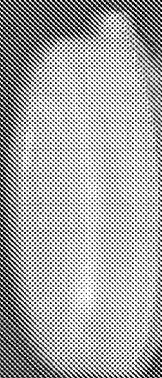
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2		10% DS	1.0% SDS (A)	0	0	solution	precipitate	
3		20% DS	1.0% SDS (A)	0	0	solution	precipitate	
4		30% DS	1.0% SDS (A)	0	0	solution	precipitate	
5		Sat. DS	1.0% SDS (A)	0	0	solution	precipitate	
6		water	3.0% SDS (A)	0	0	solution	transparent	
7		10% DS	3.0% SDS (A)	0	0	solution	precipitate	
8		20% DS	3.0% SDS (A)	0	0	solution	precipitate	
9		30% DS	3.0% SDS (A)	0	0	solution	precipitate	
10		Sat. DS	3.0% SDS (A)	0	0	solution	precipitate	
11		water	1.0% Cetri Cl (C)	0	0	solution	transparent	
12		10% DS	1.0% Cetri Cl (C)	0	0	solution	precipitate	
13		20% DS	1.0% Cetri Cl (C)	0	0	solution	precipitate	
14		30% DS	1.0% Cetri Cl (C)	0	0	solution	precipitate	
15		Sat. DS	1.0% Cetri Cl (C)	0	0	solution	precipitate	
16		water	5.0% Cetri Cl (C)	0	0	solution	transparent	
17		10% DS	5.0% Cetri Cl (C)	0	0	solution	precipitate	
18		20% DS	5.0% Cetri Cl (C)	0	0	solution	precipitate	
19		30% DS	5.0% Cetri Cl (C)	0	0	solution	precipitate	
20		Sat. DS	5.0% Cetri Cl (C)	0	0	solution	precipitate	
21		water	1% Tween20 (N)	0	0	solution	transparent	
22		10% DS	1% Tween20 (N)	0	0	solution	transparent	
23		20% DS	1% Tween20 (N)	0	0	solution	transparent	
24		30% DS	1% Tween20 (N)	0	0	solution	transparent	
25		Sat. DS	1% Tween20 (N)	0	0	solution	transparent	
26		water	5% Tween20 (N)	0	0	solution	transparent	
27		10% DS	5% Tween20 (N)	0	0	solution	transparent	
28		20% DS	5% Tween20 (N)	0	0	solution	transparent	
29		30% DS	5% Tween20 (N)	0	0	solution	transparent	
30		Sat. DS	5% Tween20 (N)	0	0	solution	transparent	
31		water	1% Tween80 (N)	0	0	solution	transparent	
32		10% DS	1% Tween80 (N)	0	0	solution	transparent	
33		20% DS	1% Tween80 (N)	0	0	solution	transparent	

34	30% DS	1% Tween80 (N)	0	0	solution	transparent	9
35	Sat. DS	1% Tween80 (N)	0	0	solution	transparent	7
36	water	5% Tween80 (N)	0	0	solution	transparent	10
37	10% DS	5% Tween80 (N)	0	0	solution	transparent	16
38	20% DS	5% Tween80 (N)	0	0	solution	transparent	16
39	30% DS	5% Tween80 (N)	0	0	solution	transparent	46
40	Sat. DS	5% Tween80 (N)	0	0	solution	transparent	45
41	water	5% Tween20 (N)	0	0	solution	clear	60
42	10% DS	5% Tween20 (N)	0	0.4% vitamin E acetate	solution	clear	77
43	20% DS	5% Tween20 (N)	0	0.4% vitamin E acetate	solution	clear	130
44	30% DS	5% Tween20 (N)	0	0.4% vitamin E acetate	solution	clear	62
45	Sat. DS	5% Tween20 (N)	0	0.4% vitamin E acetate	solution	turbid	141
46	water	5% Tween20 (N)	0	0.6% vitamin E acetate	solution	turbid	150
47	10% DS	5% Tween20 (N)	0	0.6% vitamin E acetate	solution	turbid	165
48	20% DS	5% Tween20 (N)	0	0.6% vitamin E acetate	solution	turbid	160
49	30% DS	5% Tween20 (N)	0	0.6% vitamin E acetate	solution	clear	38
50	Sat. DS	5% Tween20 (N)	0	0.6% vitamin E acetate	solution	clear	40
51	water	5% Tween20 (N)	0	0.8% vitamin E acetate	solution	clear	62
52	10% DS	5% Tween20 (N)	0	0.8% vitamin E acetate	solution	clear	77
53	20% DS	5% Tween20 (N)	0	0.8% vitamin E acetate	solution	clear	84
54	30% DS	5% Tween20 (N)	0	0.8% vitamin E acetate	solution	clear	40
55	Sat. DS	5% Tween20 (N)	0	0.8% vitamin E acetate	solution	clear	82
56	water	5% Tween80 (N)	0	0.4% vitamin E acetate	solution	clear	80
57	10% DS	5% Tween80 (N)	0	0.4% vitamin E acetate	solution	clear	89
58	20% DS	5% Tween80 (N)	0	0.4% vitamin E acetate	solution	clear	91
59	30% DS	5% Tween80 (N)	0	0.4% vitamin E acetate	solution	clear	46
60	Sat. DS	5% Tween80 (N)	0	0.4% vitamin E acetate	solution	clear	90
61	water	5% Tween80 (N)	0	0.6% vitamin E acetate	solution	clear	95
62	10% DS	5% Tween80 (N)	0	0.6% vitamin E acetate	solution	clear	
63	20% DS	5% Tween80 (N)	0	0.6% vitamin E acetate	solution	clear	
64	30% DS	5% Tween80 (N)	0	0.6% vitamin E acetate	solution	clear	
65	Sat. DS	5% Tween80 (N)	0	0.6% vitamin E acetate	solution	clear	
66	water	5% Tween80 (N)	0	0.8% vitamin E acetate	solution	clear	
67	10% DS	5% Tween80 (N)	0	0.8% vitamin E acetate	solution	clear	
68	20% DS	5% Tween80 (N)	0	0.8% vitamin E acetate	solution	clear	
69	30% DS	5% Tween80 (N)	0	0.8% vitamin E acetate	solution	clear	

104	30% DS	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	10
105	Sat. DS	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	10
106	water	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	13
107	10% DS	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	14
108	20% DS	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	16
109	30% DS	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	12
110	Sat. DS	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	16
111	water	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.8% vitamin E acetate	gel	clear	42
112	10% DS	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.8% vitamin E acetate	gel	clear	26
113	20% DS	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.8% vitamin E acetate	gel	clear	29
114	30% DS	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.8% vitamin E acetate	gel	clear	30
115	Sat. DS	1.5%A650+1.5%T80(N)	OH-ethylcellulose	0.8% vitamin E acetate	gel	clear	39
116	water	3% Ariatone 975 (N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	40
117	10% DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	55
118	20% DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	38
119	30% DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	33
120	Sat. DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	36
121	water	3% Ariatone 975 (N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	47
122	10% DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	68
123	20% DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	46
124	30% DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	43
125	Sat. DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	41
126	water	3% Ariatone 975 (N)	OH-ethylcellulose	0.8% vitamin E acetate	gel	clear	70
127	10% DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.8% vitamin E acetate	gel	clear	92
128	20% DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.8% vitamin E acetate	gel	clear	65
129	30% DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.8% vitamin E acetate	gel	clear	60
130	Sat. DS	3% Ariatone 975 (N)	OH-ethylcellulose	0.8% vitamin E acetate	gel	clear	63
131	water	1.5%A975+1.5%T20(N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	11
132	10% DS	1.5%A975+1.5%T20(N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	11
133	20% DS	1.5%A975+1.5%T20(N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	8
134	30% DS	1.5%A975+1.5%T20(N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	8
135	Sat. DS	1.5%A975+1.5%T20(N)	OH-ethylcellulose	0.4% vitamin E acetate	gel	clear	9
136	water	1.5%A975+1.5%T20(N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	15
137	10% DS	1.5%A975+1.5%T20(N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	18
138	20% DS	1.5%A975+1.5%T20(N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	16
139	30% DS	1.5%A975+1.5%T20(N)	OH-ethylcellulose	0.6% vitamin E acetate	gel	clear	16

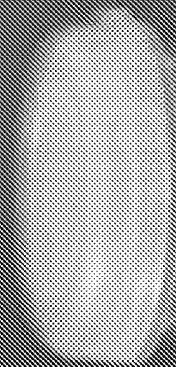
174	F129 Photo 4C	75% DS	6.25% BC (C)	0.4% Natrasol	0.2% vitamin E acetate	solution	turbid
175		sea	6% Tween 20 (N)	0	0	solution	clear
176		30% DS	6% Tween 20 (N)	0	0	solution	clear
177		50% DS	6% Tween 20 (N)	0	0	solution	clear
178		80% DS	6% Tween 20 (N)	0	0	solution	clear
179	F115 Photo 5A	80% DS	6% Tween 20 (N)	0	0.2% vitamin E acetate	solution	clear
180	F117 Photo 5B	80% DS	6% Tween 20 (N)	0	0.4% vitamin E acetate	solution	clear
181	F143 Photo 5C	50% DS	6% Tween 20 (N)	0	0.2% vitamin E acetate	solution	clear
182	F144 Photo 6A	50% DS	6% Tween 20 (N)	0.4% Natrasol	0.2% vitamin E acetate	gel	clear
183	F128 Photo 6B	80% DS	6% Tween 20 (N)	0.4% Natrasol	0.2% vitamin E acetate	gel	clear
184	F115 Photo 7A	80% DS	6% Tween 20 (N)	0	0.2% vitamin E acetate	solution	clear
185	F117 Photo 7A	75% DS	6.25% BC (C)		0.2% vitamin E acetate	clear	clear
186	F116 Photo 7B	80% DS	6% Tween 20 (N)	0	0.2% vitamin E acetate	solution	turbid
187	F118 Photo 7B	75% DS	6.25% BC (C)	0	0.4% vitamin E acetate	solution	clear
188	F128 Photo 8,8A	80% DS	6% Tween 20 (N)	0.4% Natrasol	0.2% vitamin E acetate	gel	turbid
189	F129 Photo 8,8A	75% DS	6.25% BC (C)	0.4% Natrasol	0.2% vitamin E acetate	gel	clear
190	F144 Photo 9	50% DS	6% Tween 20 (N)	0.4% Natrasol	0.2% vitamin E acetate	gel	clear
191	F142 Photo 9	50% DS	6.25% BC (C)	0.4% Natrasol	0.2% vitamin E acetate	gel	turbid
192	F147	sea	0.05% BC (C)	4% Na alginate	1% castor oil	gel	overscale
193	F148	sea	0.05% BC (C)	4% Na alginate		gel	718
194	F149	80% DS	6% Tween 20 (N)	0.4% Natrasol	0.2% vitamin E acetate	gel	relatively clear
195	F150	75% DS	6.25% BC (C)	0.4% Natrasol	0.2% vitamin E acetate	gel	97
196	F151	50% DS	6% Tween 20 (N)	0.4% Natrasol	0.2% vitamin E acetate	gel	1200; 920
197	F152	50% DS	6.25% BC (C)	0.4% Natrasol	0.2% vitamin E acetate	gel	94
198	F153	sea	0.1% BC (C)	6% Na alginate	0.2% vitamin E acetate	gel	800; 363
199	F154	sea	0.1% BC (C)	6% Na alginate	1% castor oil	gel	1600
200	F155	93.4% sea	6% Tween 20 (N)	0.4% Natrasol	0.2% vitamin E acetate	gel	overscale
201	F156	93.15% sea	6.25% BC (C)	0.4% Natrasol	0.2% vitamin E acetate	gel	22
							45

Photograph 1



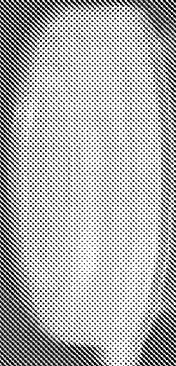
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A



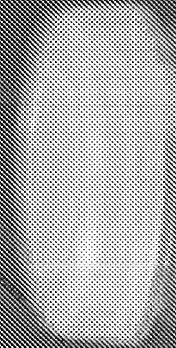
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B



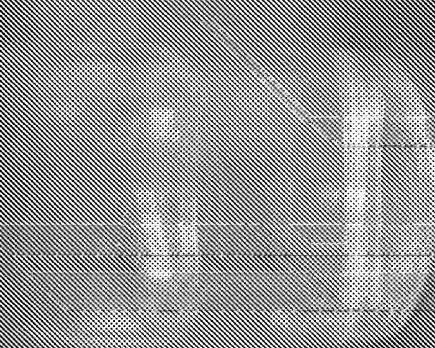
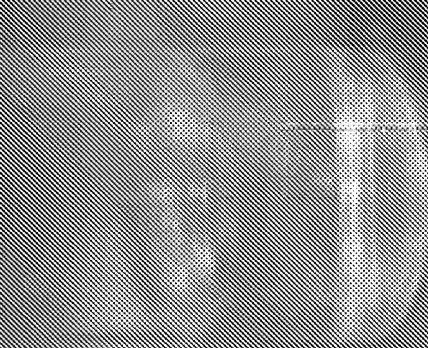
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C

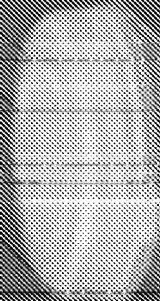


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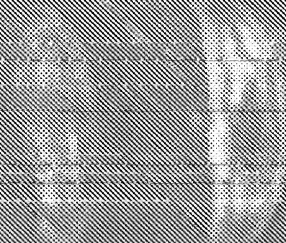
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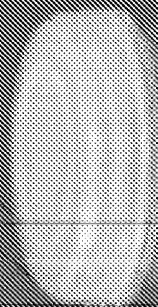
Photograph 2



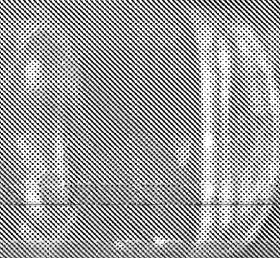
F135



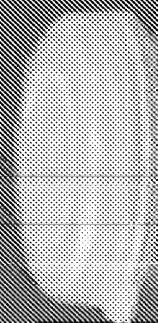
A



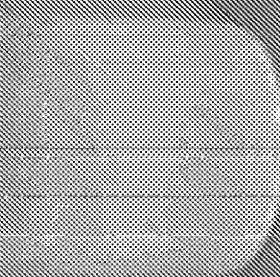
F136



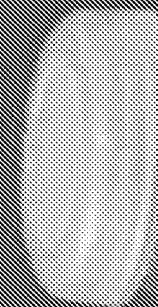
B



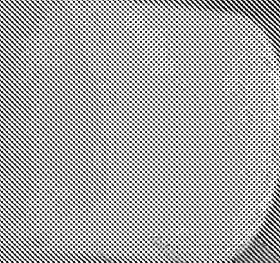
F137



C

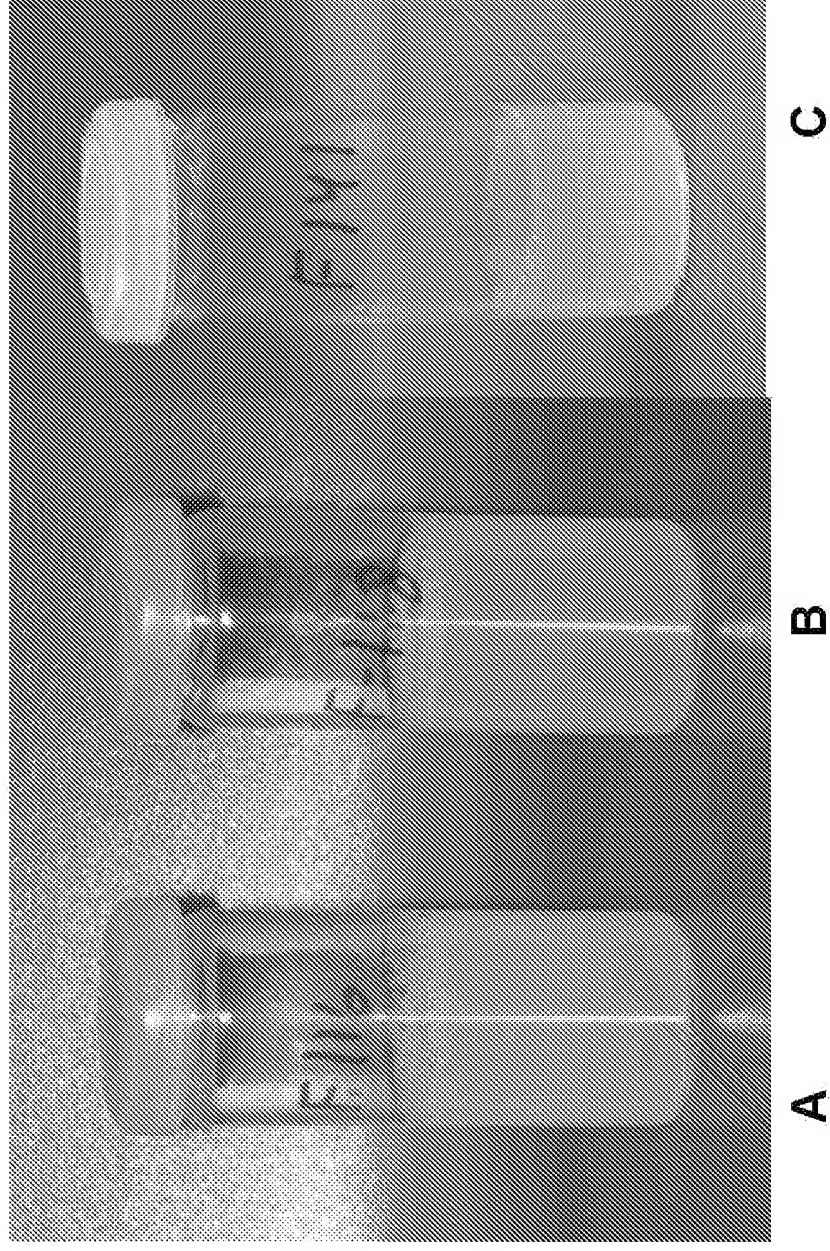


F138



D

Photograph 3



Photograph 4



A

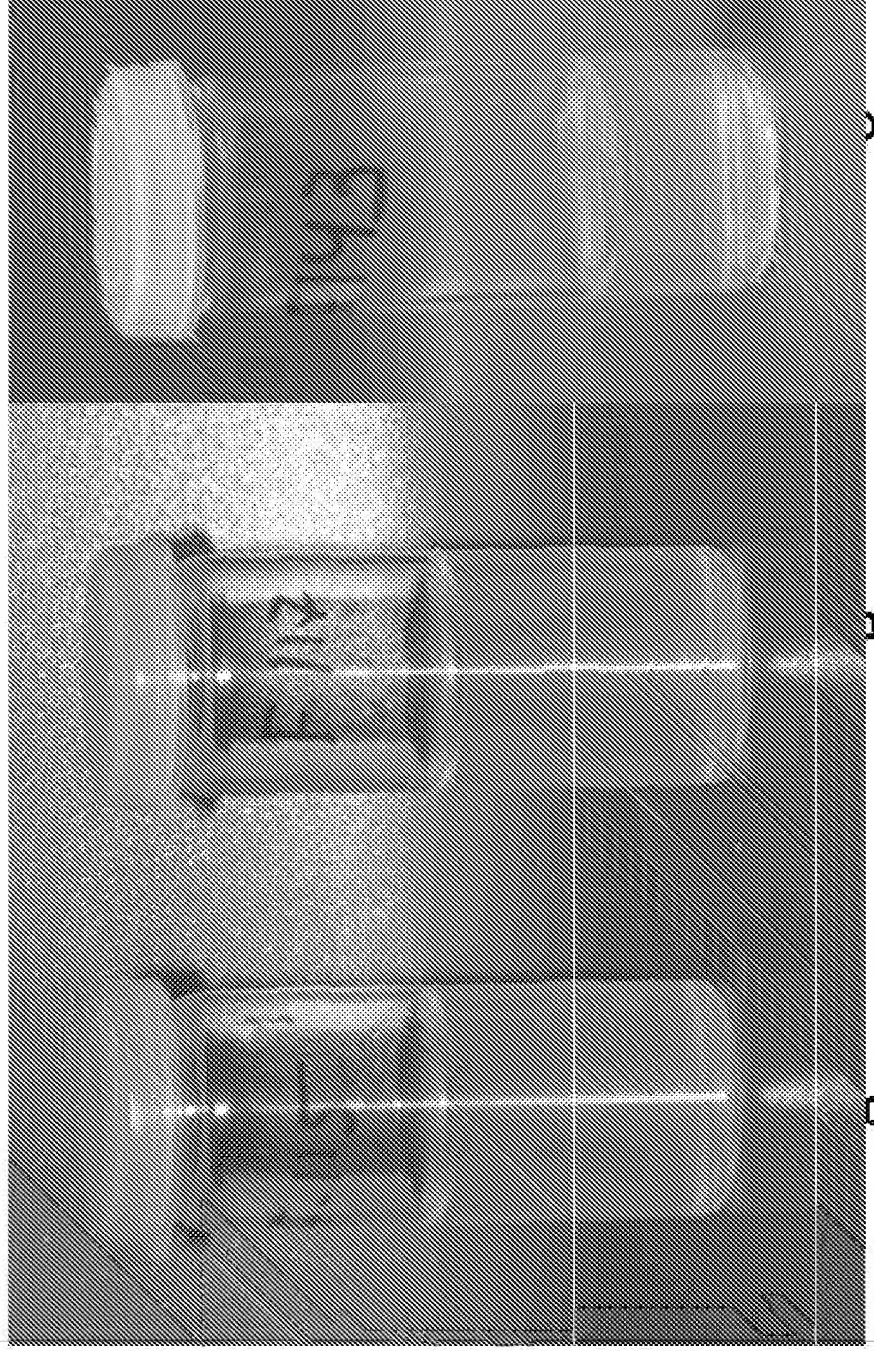


B

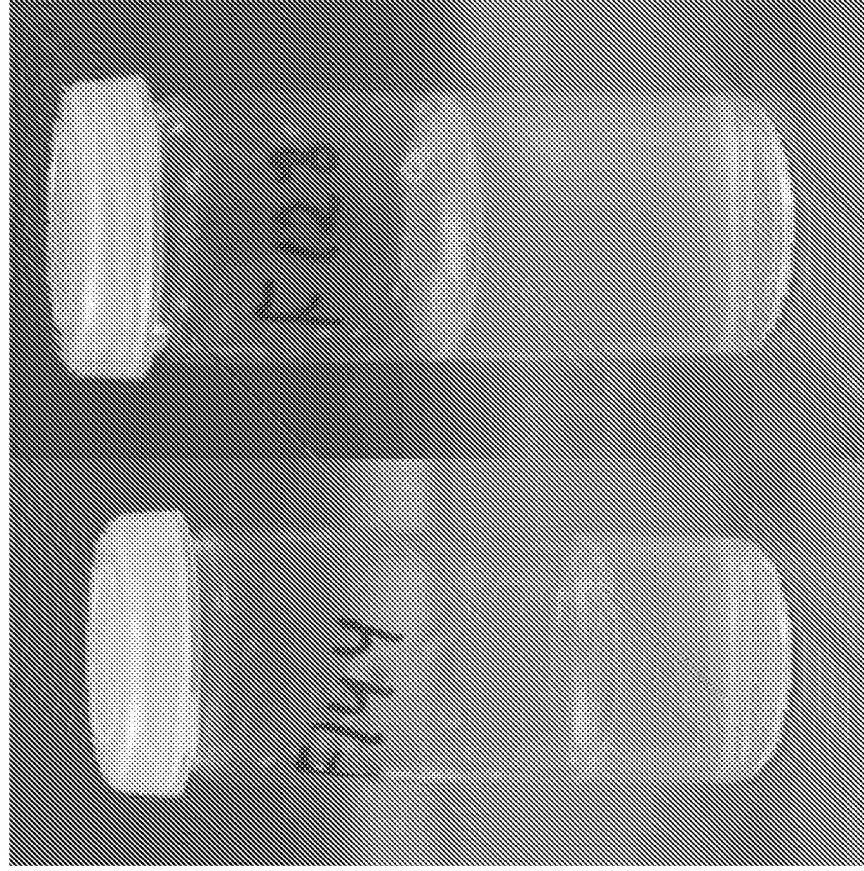


C

Photograph 5



Photograph 6



A

B

Photograph 7



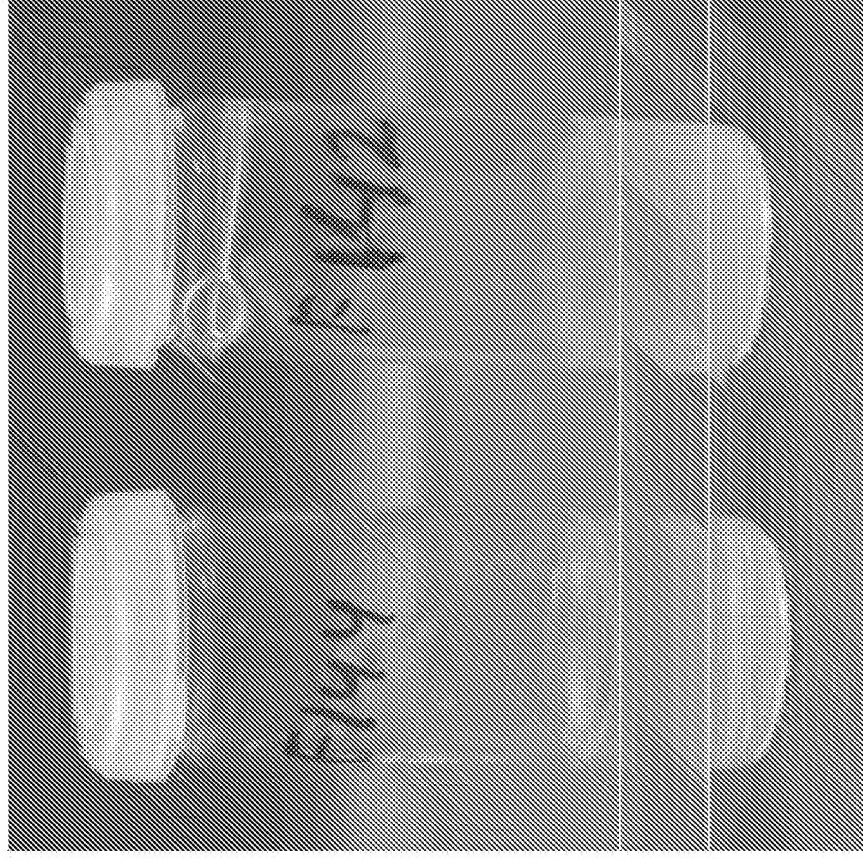
Photograph 8



BC

Tween 20

Photograph 9



Photograph 8A

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